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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/926,375	02/28/2002	Cecil W. Forsberg	6580-270	9974

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EXAMINER

BERTOGLIO, VALARIE E

ART UNIT	PAPER NUMBER
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1632

DATE MAILED: 08/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/926,375

Applicant(s)

FORSBERG ET AL.

Examiner

Valarie Bertoglio

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05/27/05.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19,22-24,27-31 and 33-57 is/are pending in the application.
- 4a) Of the above claim(s) 36-57 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11,13-17,19,22-24,27-31 and 33-35 is/are rejected.
- 7) ☐ Claim(s) 12 and 18 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 10/23/2001 is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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Art Unit: 1632

DETAILED ACTION

Applicant's reply filed 05/27/2005 has been received. Claims 1, 2, 10, 11, 13, 17, 19, 22, 23, 27, 30 and 34 have been amended. Claims 20,21,25,26 and 32 are cancelled. Claims 36-57 are withdrawn. Claims 1-19,22-24,27-31 and 33-57 are pending and claims 1-19,22-24,27-31 and 33-35 are under consideration in the instant office action.

Specification

The objection to the specification is withdrawn in light of Applicants' amendments deleting hyperlinks.

Sequence Compliance

The amendment to the specification dated 09/12/2003 is acknowledged. Accordingly, the failure to comply with the sequence requirements is withdrawn.

Claim Objections

The objection to claim 13 is withdrawn in light of Applicants' amendment to the claim.

Claims 1,13 and 19 are objected to because of the following informalities: The preamble of claim 1 is drawn to a non-human animal; however, the body of the claim is limited to specific mammalian species. Therefore, the preamble is not consistent in scope with the body of the claim. As such, the claim should read "A transgenic non-human mammal".

Appropriate correction is required.

Double Patenting

Applicant is advised that should claim 1 be found allowable, claim 15 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. Applicant is advised that should

Art Unit: 1632

claim 3 be found allowable, claim 16 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). While the wording of the claims differ, the claimed subject matter appears to be the same. Claim 15 requires a salivary specific promoter, which by definition, limits the general expression of claim 16 to expression in the salivary gland.

Claim Rejections - 35 USC § 112-1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11,13-17,19,22,24, 27,29-31 and 33-35 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a transgenic non-human mammal whose genome comprises a transgene comprising a gene encoding a phytase operably linked to a mammalian salivary gland specific promoter wherein the mammal is a pig, goat, sheep, cow, or horse, wherein the phytase is expressed in the salivary gland and secreted into the saliva of the mammal does not reasonably provide enablement for any other animal encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Art Unit: 1632

Applicant's arguments have been thoroughly considered and are partially persuasive.

Aspects of the rejection are withdrawn as set forth below. Furthermore, new grounds of rejection are also presented below,

The claims were previously rejected on three grounds. First, the claims encompassed non-mammalian species including fish and birds, which are not enabled by the specification in light of the unpredictability associated with the art of making transgenic fish and birds, the lack of conservation of salivary promoters and the lack of guidance in the specification (see pages 9-10 of the office action mailed 02/28/05). Second, the claims fail to require transgene expression in the salivary glands. The specification fails to enable using mammals that fail to express the transgene and fails to enable making the claimed mammals using a salivary specific promoter wherein expression occurs anywhere other than in the salivary gland (see pages 10-11 of the office action mailed 02/28/05). Third, the specification is not enabling for the claimed mammal wherein the transgene encodes any protein or any glycoprotein (see page 11 of the office action mailed 02/28/05). This third aspect of the rejection, relating to claims 1-9,11, 19-25,29-32 and 35, is withdrawn in light of Applicant's amendments to the claims.

The first aspect of the rejection is withdrawn as it relates to claims 1-19,22-24 and 27-29; however, it is maintained as it relates to claims 15 and 30,31 and 33-35. Claim 15 continues to encompass use of non-mammalian salivary specific regulatory sequences that do not predictably have the expected activity in mammalian cells (see page 8-9 of the office action mailed 02/28/2005). Applicant has limited the animal species of claims 1-19,22-24 and 27-29 to mammalian species including pigs, goats, sheep, cow and horse. However, claims 30-35 fail to recite a similar limitation and encompass non-mammalian species, including fish and birds. The

Art Unit: 1632

rejection is maintained for claims 15 and 30,31 and 33-35 for reason of record set forth at pages 8-10 of the office action mailed 02/28/05.

With respect to the second grounds of rejection based on the failure of the claims to require transgene expression, Applicant has amended claims 1 and 13 to require that the phytase gene be expressed (claims 13 and 14) in the salivary glands (claims 1-12,15,16,19,22,23,24,27-29). Claim 17 merely limits the general expression limitation of claim 13 to the salivary gland or gastrointestinal tract in general. However, claims 15 and 16 limit the transgene of claim 13 to those comprising salivary specific regulatory sequences, effectively limiting expression to the salivary glands. Claim 19 is also broad in requiring expression or secretion in the gastrointestinal tract; however, the claim required a salivary specific regulatory sequence, effectively limiting expression to the salivary glands and obviating this aspect of the rejection for claims 19,22,23,24 and 27-29. Applicant has additionally argued that post-filing art demonstrates that a specific embodiment of the claims, the Lama2 promoter/enhancer construct is expressed in other areas of the gastrointestinal tract (pages 11-12 of Applicants' remarks). These amendments and arguments are not persuasive as they relate to claims 13,14, and 17.

In response, the specification, as filed, provides no evidence that the promoters described in the specification would have activity anywhere in the gastrointestinal tract other than the salivary glands. Post-filing art fails to support that the inventors were in possession of such breadth at the time of filing and the specification, therefore, was not enabling for expression of phytase anywhere other than that taught in the specification, which is in the salivary gland. Furthermore, evidence that one specific promoter expresses in tissues other than salivary glands

Art Unit: 1632

does not provide similar support for other promoters encompassed by the genus of salivary-specific promoters. Therefore, the rejection is maintained as it relates to claims 13,14 and 17

A new ground of rejection appears below.

The specification fails to enable one of ordinary skill in the art to use the methods or the transgenic animal of claims 1-11,13-17,19,22-24 and 29. Claims 1-11,13-17,19,22-24 and 29 are not enabled because they fail to require that the transgene encode a secretion signal sequence and fail to require that the phytase gene product be secreted. The purpose of the invention is to provide phytase enzyme within the digestive tract of an animal such that it is available to hydrolyze phytate present in the food the animal eats. If the phytase is not secreted, it will not have access to the food. Therefore, the specification fails to teach one of skill in the art to use the claimed animal wherein phytase is not secreted or wherein the transgene does not encode a secretion signal sequence.

Claims 1-11,13-17, fail to require that the phytase in the salivary gland be secreted and fail to require that the transgene contain a signal sequence effective for secretion in mammalian cells. Claims 10 and 27 require that the phytase be the E. Coli AppA gene product, however, it does not necessarily require that the encoded phytase comprise the natural secretion signal sequence described at page 20 of the specification. Claim 19 requires either secretion or expression of phytase while dependent claim 23 is limited to expression. Therefore, claims 19 and 22-24 do not require secretion of phytase as they optionally require expression without secretion, and do not require a secretion signal sequence. However, claims 12,18 and 28 require that the transgene be those specifically used in the instant specification, which comprise signal

Art Unit: 1632

sequences effective in mammalian cells. As such, claims 12,18 and 28 are not included in this rejection.

The state of the art at the time of filing held that certain phytases were not secreted in heterologous species using the natural phytase coding sequences. For example, Li et al. demonstrated that an exogenous signal sequence was necessary for secretion of a fungal phytase from soybean cells [**Plant Physiol.**, 114:1103-1111,1997, specifically page 1107, col. 1, last paragraph). Hong et al. also added exogenous sequences to allow for secretion of bacterial phytases in rice seeds [**Transgenic Research**, 13:29-39,2004]. Therefore, not all phytases would be expected to be secreted from the cells of the claimed animals without the inclusion of a secretory signal sequence. Without a requirement for secretion of phytate, the skilled artisan would not know how to use the claimed invention.

Therefore, claims should require that the transgene encode a secretion signal sequence operably linked to the phytate gene product and that the phytate be expressed and secreted.

Claim Rejections - 35 USC § 112-2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 19,22,24,27-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The following new rejection is necessitated by the amendments to the claims.

Claims 19,22,24,27-29 are unclear because, as amended, they require a salivary specific promoter in the body of the claim, however, the preamble as well as the body of the claims also

Art Unit: 1632

require broader gastrointestinal expression that is not consistent with “at least one mammalian regulatory sequence for salivary gland specific expression”. Therefore, it is not clear if Applicant has intended to narrow the scope of the claim to expression in the salivary gland or is attempting to claim only salivary-specific promoters that express in other parts of the gastrointestinal tract. If the latter is the case, then the metes and bounds of “salivary gland specific expression” are not clear as the phrase is not defined by the specification and, based on the broad “gastrointestinal” terminology of the claim, does not appear to be drawn to the literal definition of the term “specific”.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

1) The rejection of claims 1-5,8,19-25,29-32 and 35 under 35 U.S.C. 103(a) as being unpatentable over Mikkelsen (1992) in view of Velander (1992) is withdrawn in light of Applicant's arguments regarding the expectation of success in expressing phytase in the digestive system of large mammals as well as the limitation of the claims to a transgene encoding phytase. Neither Mikkelsen nor Velander taught phytase.

Art Unit: 1632

2) Claims 30 and 34 remain rejected and claims 31,33 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mikkelsen (1992) in view of Velandar (1992) and further in view of Pen (1993) as evidenced by Laursen (1997).

Applicant's arguments have been fully considered and are not persuasive as they relate to claims 30 and 34. Applicant has argued, as set forth above, that, at the time of filing, there was not a reasonable expectation of success of carrying out the claimed invention in large mammals because phytase had not been successfully expressed in large animals to effectively hydrolyze phytate. However, claims 30 and 34 are not limited to large mammals and do not require expression to levels effective in digestion/hydrolysis of phytate. Claims 30 and 34 are merely drawn to isolation of phytase and one of skill in the art would have a reasonable expectation of success in expressing the phytase transgene to levels sufficient for protein isolation. The art applies similarly to claims 31,33 and 35 that were omitted from the rejection as set forth at pages 13-15 of the office action dated 02/28/2005.

The rejection is withdrawn as it relates to claims 1,10,11,13-17,19,26 and 27 in light of Applicant's arguments regarding the expectation of success in expressing phytase in the digestive system of large mammals (pages 12-14 of Applicant's reply).

Allowable Subject Matter

Claims 12 and 18 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Art Unit: 1632

Claim 28 would be allowable if rewritten to overcome the rejection(s) under 35

U.S.C. 112, 2nd paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Art Unit: 1632

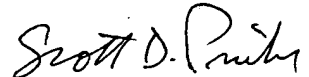
Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Valarie Bertoglio
Examiner
Art Unit 1632



SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER